

Brain Trust: The Hidden Connection Between Mad Cow and Misdiagnosed Alzheimer's Disease by Colm A. Kelleher. Paraview Pocket Books, 2004. 312 pp. \$22.00 US, \$32.00 Canada (hardcover). ISBN 0-7434-9935-2.

Brain Trust, by Colm A. Kelleher, is a troubling book.

It is troubling, first, because of the subject matter. Kelleher's topic is the relatively new (at least to science) family of brain-wasting diseases known as transmissible spongiform encephalopathies (TSEs). Specific animal TSEs include the bovine affliction BSE, or "Mad Cow Disease," which has devastated the British and European cattle industries; scrapie, a disease of sheep known for more than two centuries; Chronic Wasting Disease (CWD), which is killing North American deer and elk; and a variant seen in farmed mink (TME), which may be linked, through the mink's feed, to an endemic but undocumented North American variety of BSE. The two best-known human TSEs are kuru, which infected the Fore tribe of New Guinea and was spread by cannibalism, and Creutzfeldt-Jacob Disease (CJD). The latter has been known for decades primarily as a "sporadic" disease of undetermined origin, with less common iatrogenic and familial strains. Since 1996, though, a so-called "new variant" CJD (vCJD), with more than 150 victims thus far in the UK and Europe, has been attributed to eating meat from BSE-infected cows.

The TSEs are disturbing both because they are invariably fatal and because so much is still unknown about their presumptive causative agents, mutant proteins known as prions, and the modes of transmission of the TSEs between and within species. Kelleher argues that BSE and CWD are widespread in North America and represent a much more serious public health threat than the authorities have been willing to acknowledge. He makes a forceful case for more aggressive research and stronger regulatory measures to contain the "epidemic" before it spreads out of control.

Brain Trust is troubling for another reason as well: It is a book of terribly uneven quality. Several chapters show off the author's precise grasp of nuanced scientific issues and his skill as both a reporter and a story-teller. The book is highly readable, and for those not already familiar with the scientific side of the story it is an easily digested but by no means superficial guide to the current state of knowledge. But other sections of the book are deeply flawed, because the author steps away from scientific, objective reporting and engages in passionate advocacy. In sounding the alarm about what he believes to be the public health threats of TSEs, Kelleher resorts repeatedly to overheated rhetoric and one-sided analysis and occasionally slips into fear-mongering sensationalism.

Several chapters also eschew critical examination of evidence and promote Kelleher's own theories. Those theories—that there is a "hidden epidemic" of CJD, misdiagnosed as Alzheimer's disease; that TSEs have spread throughout North American wildlife after originating from prion-carrying test animals at an NIH research facility in Patuxent, MD, in the 1960s and '70s; and that cow mutilations, a bizarre phenomenon that has occurred since the 1960s, represent

a covert monitoring program to check for the presence of TSEs in North American cattle—might each, arguably, be worth debating. But when Kelleher sets aside his reportorial role to press these theories, he adds a further emotional, biased tone to the book and diminishes its overall credibility.

That is unfortunate, because the book does have much to recommend it. For those who have read Richard Rhodes' *Deadly Feasts* (1997), the scientific detective story will be a familiar one, but Kelleher re-tells and updates it well here. He guides readers through the investigations of *kuru* in New Guinea by Carleton Gajdusek and others; the discovery that *kuru* and scrapie were essentially identical diseases; the experiments at Patuxent and in the UK that showed that both diseases were caused by an infectious agent that could be transmitted from species to species; and the work by Stanley Prusiner and others that finally identified the agent as a misfolded cellular protein, dubbed by Prusiner in 1982 a "prion" (pronounced pree-on). The mutant prions induce their own replication in brain cells and ultimately leave sponge-like vacuoles throughout the brain. The science of TSEs is truly fascinating (Gajdusek and Prusiner were each, separately, awarded the Nobel Prize for their work), and Kelleher's account conveys the excitement of discovery.

Kelleher also does a fine job of documenting the BSE debacle in the UK. He deftly intertwines narratives describing step-by-step advances in knowledge of the extent and causes of the disease and the bureaucratic decisions, compulsive secrecy, and public statements of the Ministry of Agriculture, Fisheries and Foods (MAFF), which at the time was responsible for safety of the UK food supply. These chapters document, in painful detail, the appalling cascade of MAW mistakes, from interpreting incomplete scientific evidence to reinforce their belief that there was no human health hazard, to concealing critical research data and repeating public assurances that it was safe to eat British beef. *Brain Trust* provides the best account I have seen of this object lesson in bureaucratic self-deception and betrayal of the public trust. In researching this history, Kelleher had access to internal memoranda and other documentation of MAW decision-making, which the British government, to its credit, has published on the Internet in the report of its own BSE inquiry (Government of the United Kingdom, 2000).

The UK's goal in baring its soul about its BSE tragedy was to show what went wrong and help other countries avoid the same mistakes. Kelleher is worried, perhaps with good reason, that history will repeat itself. He finds much evidence, in examining the status of BSE in the US and Canada, of the same kinds of denial, influence by regulated industries over government judgments, and public-relations campaigns aimed at defusing fears and promoting meat consumption that were observed in the UK disaster. But the chapters on mad cow disease in North America are among the weakest in the book.

In contrast to his meticulous reporting on the step-by-step march to self-destruction of MAFF in the UK, Kelleher's investigation of the US's response to BSE is superficial and seriously misleading. He relies heavily on secondary

sources—newspaper stories and the muckraking *Mad Cow USA*, by Sheldon Rampton and John Stauber (1997). Like that book, Kelleher's is replete with allegations that former cattle and beef industry officials control policy at the US Department of Agriculture (USDA) and with invective about a crisis swept under the rug to protect industry profits. But because of either shallow research or conscious omission, Kelleher fails to describe the US Food and Drug Administration (FDA)'s 1997 regulation on animal feeding practices, adopted to prevent exactly the scenario—cow cannibalism, the feeding of rendered cattle remains back to cattle—that magnified BSE in the UK to its epidemic proportions. Because that regulation was in place in North America before BSE had been officially detected at all—and certainly at a time when it could not have been very widespread—the critical ingredients for a repeat of the British disaster appear not to be present here. This point seems to escape Kelleher, who argues strenuously to the contrary—i.e., he believes BSE is epidemic in US cattle but has either gone undetected or is being concealed by the authorities.

This is not to say that the US response has been adequate. Public-interest advocates have long pressured the FDA, and the USDA inspection agency that oversees slaughterhouses, for tighter regulations and have complained with some merit that the economic interests of the powerful cattle, meat, and rendering industries often seem to trump concerns about public health. In a later chapter about the first officially recognized BSE case in the US (in December 2003), Kelleher notes that FDA and USDA used that event as an excuse to propose closing several loopholes in the animal feeding and slaughterhouse regulations (although to date most of them remain unclosed). Readers may find this reference to US regulations puzzling, because earlier chapters never describe those regulations.

Kelleher's review of the US government's response to BSE is strongly tilted towards the polemical, designed to ratchet up the public's sense of urgency about the problem. Thus, he focuses on outrages, such as the beef industry's SLAPP lawsuit against Oprah Winfrey for hosting a discussion of BSE on her TV talk show. He also attacks the integrity of the USDA's laboratory that tests cow brains for BSE, quoting an unnamed veterinarian who hints that the lab is incompetent or corrupt and that BSE is "epidemic" in US cattle. The source of this highly charged accusation is a news article—Kelleher reports no effort of his own to validate the claim, despite its obvious potential for emotional impact. Without judging the truthfulness of the allegations, the subject is critical enough that Kelleher was remiss not to research it more thoroughly and objectively.

Largely by what he omits, Kelleher implies and sometimes argues overtly that "nothing has been done" (to contain BSE in the US). That simply is not true. The issue needing debate is whether what *has* been done is adequate, and if not, what more needs to be done. But by abandoning fair reporting in favor of a polemic argument and ignoring crucial facts, Kelleher makes his own biases the issue and undercuts his goal of stimulating debate on fundamental public policy questions.

That probably is the book's most serious flaw. In contrast to his superficial and slanted treatment of BSE in the US, Kelleher does a much better job reporting on the discovery and inexorable spread of CWD, which has long infected domestic and wild cervids (deer and elk) in the Western US and Canada and now appears to be moving eastward into Midwestern deer herds. This highly readable account gives an excellent summary of the US's "other" TSE problem. Kelleher examines the possibility that the few known cases of "sporadic" CJD in deer hunters may be caused by CWD, just as vCJD in European beef eaters was traced back to BSE. He concludes (correctly, in my view) that there is not yet enough good evidence to convincingly forge that link, but he flags this as an important question for research and castigates US health authorities for not taking the risk more seriously.

Kelleher's chapter on CWD addresses another pivotal question for research: Can CWD jump from deer and elk into cattle? The answer is far from clear at this point, but *Brain Trust* expresses justifiable concern about the possibility, which would be consistent with some experimental data. If so, CWD probably poses a greater danger to the US beef and cattle industries than the occasional import of a BSE-positive cow from Canada.

In contrast to his perceptive account of CWD, Kelleher's chapters promoting his own sometimes-tenuous theories about TSEs are each, to varying degrees, weak points that could undermine the book's hoped-for impact. The most interesting and plausible of these chapters, hinted at in the book's subtitle, explores frequent misdiagnosis of CJD as Alzheimer's disease. Kelleher's thesis is that the true incidence of CJD is probably far higher than the widely accepted estimate of one case annually per million population. CJD can be diagnosed definitively only by autopsy; it is likely that many cases are not recorded on death certificates. Two relatively small studies have shown that 5 and 13 percent, respectively, of deaths attributed initially to either Alzheimer's disease or to non-specific dementia were actually CJD on follow-up brain autopsy. The true incidence of CJD has almost surely been understated, and better knowledge of its actual prevalence is required to support, among other things, epidemiological studies of possible causes.

This chapter would be stronger if Kelleher had explored the topic in more depth and sharpened his argument. Had he reviewed the extensive science on Alzheimer's disease more thoroughly, he might have better answered the many questions he raises—such as how much of the apparent increase in Alzheimer's disease incidence over the past several decades is due to an aging population and better detection, and what do leading researchers in the field think causes the affliction? Regarding misdiagnoses of CJD, though it is clear this occurs, this has probably always been the case, and without good historical data Kelleher's assertion that CJD incidence is sharply increasing is simply untenable. Better differentiation of CJD from Alzheimer's disease, along with better understanding of causes, could help us design more effective prevention strategies. But instead of more ambitious, solidly scientific reporting, Kelleher here falls into

alarmist sensationalism, claiming that there has been a "catastrophic increase" in Alzheimer's disease and "hidden" CJD, which he interprets as further evidence that BSE and other TSEs are widespread in the food supply.

Consider, for example, the counterproductive tone of this argument that wider testing for the presence of prions is needed: "Only [by testing] is it possible to uncover the extent of the silent catastrophic iceberg of a massive prion epidemic throughout the food chain that lurks beneath the cant, the propaganda and the bland assurances from the beef industry that eating beef is still safe" (p. 198). An important, valid scientific insight is buried beneath overwrought rhetoric that sends an anti-scientific message.

A second theory Kelleher propounds in *Brain Trust* is that the kuru-laced brains brought back to the US by Carleton Gajdusek and Joseph Smadel in the 1950s launched a wave of TSEs that still ripples through North American wildlife. The book's final chapter argues that TSEs may be hiding in multiple wildlife populations—squirrels, rabbits, raccoons, skunks, perhaps even birds and insects—because containment of experimental animals at the Patuxent Wildlife Research Center, where Gajdusek, Joe Gibbs, and others did their pioneering TSE-transmission studies, was inadequate. But, aside from one cluster of CJD cases in people who ate squirrel brains and the CWD epidemic in cervids, there is little concrete evidence that TSEs are prevalent in wildlife and virtually no evidence indicating that the Patuxent experiments might have been the origin of whatever TSEs are present. A more plausible origin for CWD is probably scrapie. Several infected flocks of sheep were documented in the US in the 1940s and '50s, before a USDA eradication program was implemented, and *Brain Trust* cites known contact between deer that developed CWD and sheep (of undocumented scrapie status) pastured on the same land.

Ultimately, this speculative hypothesis is probably unprovable, and where TSEs might have come from matters less than where they now are and how they can be contained. The primary significance of the chapter is not so much Kelleher's provocative theory, but rather the dearth of solid scientific research that invites him to propose it. Clearly, much more must be learned about prion ecology—where and how TSEs occur among wild and domestic animals, how they move around in ecosystems, how hard or easy it is for each specific TSE to be transmitted across the so-called "species barrier" (a concept Kelleher views skeptically), and so forth. Kelleher accurately points out that our lack of understanding of these basic ecological issues hobbles our ability to assess and manage the public health threat posed by TSEs.

In the chapter on cattle mutilations, *Brain Trust* takes a sharp turn into the territory of the *National Enquirer*. In the 1990s, Kelleher worked at the National Institute for Discovery Science, where he investigated the widespread, mysterious killing of cattle, accompanied by removal of organs such as the eyes, ears, tongue, reproductive organs, anus, and large intestine (but apparently not the brain). He acknowledges that Internet web sites attribute cattle mutilations to "space aliens," and that scientists who treat the topic seriously

risk subjecting themselves to ridicule, but Kelleher clearly takes this topic quite seriously and attempts to explain the mystery by linking it to TSEs. He contends that the mutilations represent a decades-long, nationwide, covert biological sampling program carried out by unknown investigators to monitor the spread of TSEs.

In laying out his thesis, Kelleher abandons scientific methods and suspends disbelief. He quotes a former Colorado sheriff's claim that "There were always strange, silent aircraft in the vicinity before and during the mutilations." He cites recent research that he says indicates that the tissues removed by the mutilators are "loaded with prions" and thus would be excellent biological samples to monitor for TSEs. He notes coincidences of time and place (cattle mutilations began in Colorado and Wyoming in the 1960s, when TME had just been linked with "downer" cows, and CWD was just starting to appear in deer herds in the same states) as a reason why someone might be checking cattle for a TSE, even though BSE, *per se*, was not yet a recognized disease.

But wait a minute. In the 1960s and '70s, when the mutilations became a phenomenon, CWD was not known to be a prion disease; prions had not been identified, and little was known about which tissues (other than the brain) the mysterious infectious agents were found in. So, not only would the "monitors" have used unearthly technology (those silent "black helicopters"), but their understanding of prion biology also would have needed to be many years ahead of the rest of the scientific community's. Kelleher dismisses any and all alternative explanations and clearly believes fervently in what he is arguing. But by including this (frankly ridiculous) thesis in *Brain Trust*, he will indeed subject his book to ridicule and generate doubts about his judgment in the rest of his reporting.

If readers can give them any credence after his foray into the cattle mutilation minefield, *Brain Trust* offers Kelleher's recommendations for TSE research. They are generally sound proposals and deserve more attention than they are likely to get, should the book's prominent flaws permit the author's better ideas to be ignored.

Kelleher proposes, and I agree, that more extensive and intensive epidemiological study on CJD is urgently needed. CJD should be on the federal list of mandatory "reportable" diseases to support better estimates of its true incidence. He urges aggressive studies of deer hunters and venison eaters to assess the possible link between CWD and CJD—a critical question; but epidemiological studies also should look for broader connections, between eating meat of all types and CJD. One study in the US (Davanipour et al., 1985) and one in Europe (van Duijn et al., 1998) have associated pork consumption with CJD, a finding not mentioned in *Brain Trust*, and, as far as I know, not followed up with enough further research. But studies should look for any associations between animal protein in diets and CJD. We do not know enough yet to rule out the possibility of a porcine TSE (or other TSEs in food animals, including cattle) that might introduce prions into the food chain, without producing an identified

disease in the animals that carry them. Kelleher recommends testing surgically removed human organs and multiple wildlife species for mutant prions, a sound strategy; I suggest that much additional basic biological research on prion occurrence and transmission, both within and among species, should be a high priority as well. Until we know more about how TSEs behave in ecosystems, efforts to keep them out of the food chain may be misdirected.

I also agree with Kelleher that the federal government should be testing food-animal brains much more widely. Following the discovery of the first US "mad cow," the USDA has ramped up its testing of cattle brains, from about 20,000 per year to 120,000 or so. But in contrast, the Japanese government claims that it tests 100 percent of slaughtered cattle, and in Europe, about half are said to be tested. One hundred twenty thousand is roughly 1/3 of 1 percent of the 35 million cattle slaughtered annually in the US.

Kelleher makes few recommendations for regulatory policy, but I offer some of my own. For instance, why are any animal brains still allowed to be sold as human food in the US? A ban would seem to be a sensible and long-overdue precaution. The issue of how much testing government should require of cattle and other food animals for prions and TSEs is closely tied to the concept of acceptable risk. A national dialogue is needed on how safe we want to be from BSE and other TSEs. Much evidence suggests (but has not proven) that TSEs arise spontaneously in nature. With human surveillance being what it is, infected animals are likely to slip into the food and feed supply now and then, no matter how hard we try to prevent it.

Part of the required public-health protection is an effective "firewall" to ensure that such prion-carrying animals do not get ground up into protein supplements and fed back to food animals. The current containment system in the US needs upgrading. Loopholes in the feeding regulations need closing, and the rules must be effectively enforced. Neither goal is politically easy, but these are at least concrete steps to work for.

Assuming a satisfactory firewall is eventually in place, the most urgent policy question is, how vigilant must the effort to keep TSE-carrying animals out of the food supply be? If feed regulations can effectively block the feedback cycle that magnifies TSEs within the animal population, risk management can focus on minimizing human exposure to prions from any TSE carriers that go to slaughter. Realistically, we cannot expect to reduce this risk to zero, but with better science we should be able to quantify both prion exposure and the associated CJD risk and agree on a level of risk we are willing to accept. In a time of budget austerity, resources needed to prevent BSE and CJD are taken from what can be spent managing other food-related hazards—including some that are greater risks to health and life, given current knowledge. We must forge a national consensus on how safe from TSEs we can afford to be.

But in the end, we cannot define "safe enough" until we can define the risks much more precisely. Ignorance has enormous costs; just ask the US and

Canadian beef industries as they struggle to recover from loss of "BSE-free" status in the global market. So, the road map to sound public policy lies in vigorously pursuing knowledge, along the lines of the research strategy recently sketched out by a committee of the National Research Council (2004). Prion biology is both an intriguing field of science (perhaps the road will lead to further Nobel Prizes) and essential knowledge for public policy. If Kelleher's book can survive its own weaknesses and stimulate public debate, I hope it builds momentum for necessary research on this fascinating and vital topic.

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Bigfoot Exposed: An Anthropologist Examines America's Enduring Legend
 by David J. Daegling. Walnut Creek, California: AltaMira Press, 2004. 288 pp.
 \$24.95 (paper). ISBN 0-7591-0539-1.

This is a book in search of a niche. As the title suggests, Daegling is preoccupied with the examination of a "legend". Even the selection of cover art reflects his perception and portrayal of the matter as a rustic provincial phenomenon. So what does a biological anthropologist have to do with it? He concedes at the outset that much of the book deals with the *social history* of the phenomenon. Yet there is little adherence to accepted standards of historical scholarship. The shallow historical treatments are riddled with misstatements and uncritically rehearsed second-hand accounts, often filtered through the disingenuous interpretations of career skeptics, such as Michael Dennett. In fact, Daegling acknowledges that Dennett paved the way for the book. Judging by my own first-hand dealings with Dennett, this concession alone does much